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Evaluation of the HemoHue® Color Scale in Pregnancy and Postpartum Period

INAUGURAL-DISSERTATION
zur Erlangung der Doktorwürde der Zahnmedizin
der Medizinischen Fakultät
der Universität Zürich

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Zürich 2011

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1. Summary

Anaemia is frequently observed and regarded as a major risk factor during pregnancy and the postpartum period. Early diagnosis of anaemia is crucial. For anaemia detection, it is a standard procedure to test the haemoglobin level of pregnant and postpartum women. In general, this is done by way of invasive methods using capillary or venous blood. These methods incur high cost and require both qualified personnel and state of the art technical equipment. In developing countries, where anaemia is highly prevalent, there is a need for a simple test to assess the level of haemoglobin, preferably a non-invasive method. However, up to now, there exists no such reliable method.
For these reasons, the HemuHue® card was developed. The HemuHue® card (computed edited ink print design) consists of a visual analog scale of increasing nuance of red. The colour intensity of the conjunctival sack of the patient is compared with the scale of the HemuHue® card in order to estimate its haemoglobin value.

The HemoHue® card was first tested in this study on women in pregnancy and postpartum period. The study was performed with the University of Zurich. 151 pregnant women and 101 postpartum women were included. The medical student, a random nurse and the patients themselves separately used the HemoHue® card to estimate the level of haemoglobin for each patient. It was ensured that the required testing conditions were always met, i.e. the lighting conditions were favorable. To measure the accuracy of this test method, the results were compared with the results of the laboratory tests based on blood sampling (goldstandard).
The results show that the standard deviations of the differences of the haemoglobin measurements with respect to the haemoglobin measurements of the goldstandard (the laboratory blood test) of the three examiners vary within a range of 1.09 to 1.58 g/dl. 95 % of the values of the medical student are in the range of - 2.3 and +2.0 to the goldstandard, while it is - 2.7 and +2.1 for the nurses and - 3.9 and +2.3 for the patients.

The study allows the conclusion that the measurements by the HemoHue® card are good enough to get a fair estimate of the haemoglobin concentration of a patient. No differences in the accuracy of the measuring device have been found with respect to the origin of the patient. The examination carried out by the patient does not show the same accuracy as the results of the medical student or the nurses. Therefore, an informed and trained person is needed to run the analysis. With some experience the patients could also improve their test results.

The HemoHue® card is a simple, non-invasive device, which can be used everywhere, including non-clinical environments. The HemoHue® card could be a practical device for a quick and cost-effective analysis especially to differentiate patients with normal haemoglobin level from patients with a low haemoglobin level. This makes the card in particular interesting for developing countries, where laboratory facilities are limited and anaemia is highly prevalent.

2. Introduction

Anaemia is a disorder of the blood that involves a reduced erythrocyte count, haemoglobin concentration and/or haematocrit. In medical practice, it is frequently observed in pregnancy and during the postpartum period. In developed countries, the prevalence of anaemia is estimated to be 52% in pregnant women and in industrialized countries it is 23% (16). Anaemia represents an increased risk of an abnormal course of pregnancy and greater maternal and infant morbidity and mortality (1). Therefore, anaemia in pregnancy is regarded as a major risk factor during pregnancy (14).
Anaemia is defined by the CDC 1989 if the haemoglobin level is less than 11 g/dl during weeks 1 – 12 (1^{st} trimester) and weeks 29 – 40 (3^{rd} trimester) of pregnancy, and less than 10.5 g/dl during weeks 13 – 28 (2^{nd} trimester) and less than 10.0 g/dl during the post-partum period (1). Most frequently, anaemia is caused by an iron deficiency that influences a whole series of body functions of the pregnant woman. Symptoms include fatigue, a reduction in physical performance, increased cardiovascular stress, reduced thermoregulation and an increased predisposition to infection. Foetal risks of a low maternal haeomoglobin (below 9.0 g/dl) are premature births, intrauterine growth retardation and intrauterine foetal death (1).

Detection of anaemia is therefore essential during pregnancy and the postpartum period and a core element of any antenatal care program (2). The diagnosis tests are based on blood sampling and laboratory testing. To determine the concentration of haemoglobin by way of photometric device, haemoglobin must be converted into the more stable cyanhaemoglobin (12). Requiring qualified personnel and technical equipment, these procedures incur high costs. In developed countries, all these facilities to measure haemoglobin concentration are usually available. Nevertheless there is a need for a simple, non-invasive blood test method to assess the degree of anaemia for patients who need serial and urgent measurement. For developing countries, where anaemia is highly prevalent and laboratory infrastructure is incomplete, a device which is easy to use and does not require significant investment is exigently needed.

Traditionally, there are several anaemia detection devices, which are used particularly in developing countries. Among others, the assessment of clinical signs of the patient (e.g. conjuctiva pallor, tongue pallor, pallor of the area under the fingernails, the pallor of the palm of the hands), filter paper method and the use of WHO Haemoglobin Colour Scale. Moreover,

anaemia can be detected by the copper sulfate method or with a portable haemoglobinmeter (HemoCue) (4).

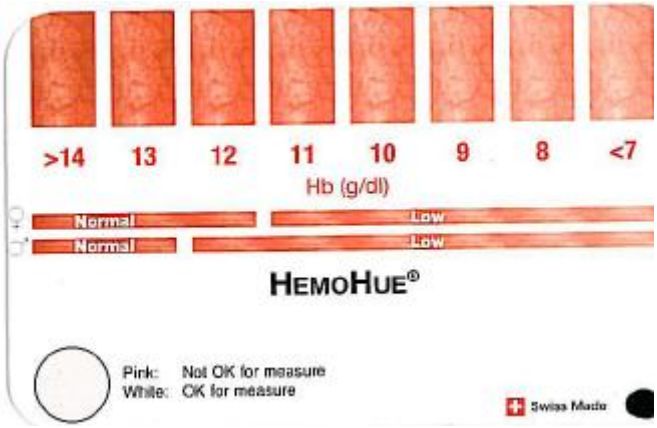
However, the above mentioned detection devices have different disadvantages in their application or lack of accuracy. As an innovative approach, HemoHue® was developed. HemoHue® is a visual analog scale which allows a standardized estimation of the degree of anaemia. It has the size of a credit card. The card features an imprinted discontinues colour scale of 7 spots with an increasing nuance of red corresponding to haemoglobin concentration values from 7 to 14g/dl. The colour intensity on the card relates to the colour intensity of the conjunctival sack. By comparing the colour of the conjunctiva with the HemoHue® colour scale, the degree of patient's haemoglobin can be assessed. This is a completely safe, painless, time-saving and particularly favorable way of examination without any risk at all. It has been proven before, that the examination of the coloration of the conjunctiva is a suitable and affordable screening method to detect anaemia (15).

The aim of the present study was to investigate both the usefulness of the HemoHue® card in predicting haemoglobin concentrations of pregnant and postpartum women and the correct handling by medical staff as well as by the women themselves.

3. Patients and Methods

3.1 HemoHue® Card

The HemoHue® card is a novel device to detect anaemia. It contains a range of digital photographs of actual standardized models of a human palpebral conjunctiva made of highly realistic textured images. To evaluate the conjunctival colour, the observer has to compare the reddest zone with the colours of the HemoHue® card. To control the steady and sufficient light conditions, a spectral power distribution metameric ink spot is integrated with the card to indicate the quality of ambient lighting. It appears white when the light conditions are good enough for testing. Therewith it is possible to visually indicate to the observer when the light conditions are insufficient for proper use of the card.



HemoHue® card: frontside with the colour scale and ink spot (left below)

HemoHue® card: backside with instructions

3.2 Patients

In this prospective study 151 pregnant women and 101 postpartum women in the University Hospital Zurich, Switzerland, were included. The research protocol was approved by The Local Committee for Research Ethics in Medicine (StV03 / 2007). All patients had been fully informed by a memorandum on the purpose of this study and accepted their participation by signature (see Appendix 7). All of them were at the age of over eighteen and understood the whole purpose of this research. Patients with acute affections of the eye and psychological disorders were excluded.

The pregnant women were visiting the hospital for their normal medical attendance (blood sampling, ultrasound, CTG etc.). In order to ensure optimal light conditions, a polychromatic neon tube was used. In this way, the study measurement could be run under steady conditions. For the estimation of haemoglobin concentrations, the examiner pulled down the lower eyelid of the patient and compared the most intensely colored zone of the conjunctival sack with one of the colour spots on the HemoHue® colour scale. The same procedure was repeated all in all by three examiners: by a medical student (running the research), by a random nurse and by the patients themselves. Every examiner acted independently from each other and did not know the haemoglobin laboratory results. The patient was only included in the research when a regular blood sampling was hold so the results could have been compared with the results of the laboratory tests. Therefore there was no need for an additional blood sampling.

The postpartum women were examined in their room in the obstetric clinic. The right ambient light conditions were verified by recognizing a white luminescent control spot on the card. All the procedures described above were repeated in the same way. During the first 14 days postpartum there is a physicological course of haemoglobin values in healthy puerperae which includes an initially short-term fall in haemoglobin level on the first day after delivery (1). For these reasons, the examination was made soonest after 24 hours past delivery.

The worksheet included women's date of birth, origin, parity, and laboratory parameters (haemoglobin, haematocrit, MCV, MCH, MCHC, and erythrocyte count). Additionally, the week of gestation and the way of delivery (spontaneous, cesarean or vaginal) were recorded in the case of pregnant women, and the blood loss in the case of postpartum women (see next page).

Worksheet

Datenerfassung – Anaemia Colour Scale

Proband Nr.	
Geburtsdatum	
Nationalität	
Alter	
Parität	
Gewicht	
SSW	
Probandenwert Hb (g/dl)	
Untersucherwert Hb (g/dl)	
Kontrollwert (Pflegeperson) Hb (g/dl)	
Schwangere: □ Risiken:	Wöchnerin: □ Art der Geburt: o spontan o Kaiserschnitt o Vaginal operativ Blutverlust: _____ Zeitpunkt der Blutentnahme: _____
Laborwerte: Hb (g/dl): _____ Hämatokrit: _____ Erythrozytenzahl: _____ Ferritin: _____	MCV: _____ MCH: _____ MCHC: _____

Datum: _____ Visum: _____

3.3 Statistics

Descriptive statistics such as mean values together with standard deviations (SD), medians, IQR, minimum and maximum are given. The goldstandard was defined as the result of the haemoglobin concentration of the blood tests. Differences between the haemoglobin measurement obtained by the medical student and the goldstandard haemoglobin measurement were computed for each woman. Similar differences were computed for the nurses and the patients.

A simple but useful semi-graphical way of summarizing data using centiles is the box-and-whisker plot. The box indicates the lower and upper quartiles and the central line is the median. The box itself contains the middle 50% of the data. The points at the end of the whiskers are 2½% and 97½% values. Several sets of data can be summarized economically using the box-and-whisker plot. Sometimes any values outside the range of the whiskers are plotted individually (3).

Bland-Altman plots were created by plotting the difference between the results received by using HemoHue® and the goldstandard, i.e. the laboratory-measured haemoglobin at y-axis and the means of the HemoHue® and the goldstandard haemoglobin measurements at the x-axis. The advantages by using the method of Bland-Altman are, in particular, that the size of differences and their distribution around the mean are much more easily to see. In addition, it is possible to check visually that the differences are not related to the size of the measurement (3).

The estimates of sensitivity, specificity, positive predictive value and negative predictive value together with the corespondable 95% confidence interval (CI) were computed in order to make our study comparable to the already existing literature. We obtained a random sample of women and we observed a random number of anaemic women equal to 32 (goldstandard). We believe that this member of anaemic women is too small in order to estimate sensitivity and positive predictive value reliably. Therefore, we do not interpret the results in detail as we are not convinced if they describe the truth reliably. Due to the small number of anaemic women, one should be cautious to interpret the results regarding the sensitivity, specificity, positive predictive value and negative predictive value.

All data were entered in an Excel file and analysed by using MedCalc (Bland-Altman plot and 95 % limits of agreement) and StatView version 5.0.1 (for the descriptive statistics and Box plots, 1 sample t-tests, 2 sample t-tests and F-test for discrepancy of variances). Statistical significance was reached at $P<0.05$. Results of the statistical analysis with p-value smaller than 5% were considered as statistically significant. The calculations were performed at the Institute of Social and Preventive Medicine of the University of Zurich, Switzerland.

4. Results

The study recruited a total of 252 women, 151 pregnant women and 101 postpartum women. The number of anaemic pregnant women is 16 (hb<11g/dl) and is 16 (hb<10g/dl) as well for postpartum women.

Most of the examined women are white origin. Black women are represented roughly by seven percent, indigen women by five percent and asian women by ten percent. The way of delivery is in the most cases spontaneous, followed by caesarean.

Table 1: Basic patient characteristics

	pregnant women	postpartum women	all
number	151	101	252
anaemic	hb < 11 g/dl 16	hb < 10 g/dl 16	32
non-anaemic	135	85	220
origin:			
- white			198
- black			17
- indigen			13
- Asian			24
mean week of pregnancy	22.9		
mean weight	68.8		
form of delivery			
- spontaneous		54	
- cesarean		34	
- vaginal operative		13	
estimated blood loss (ml)		424.9	

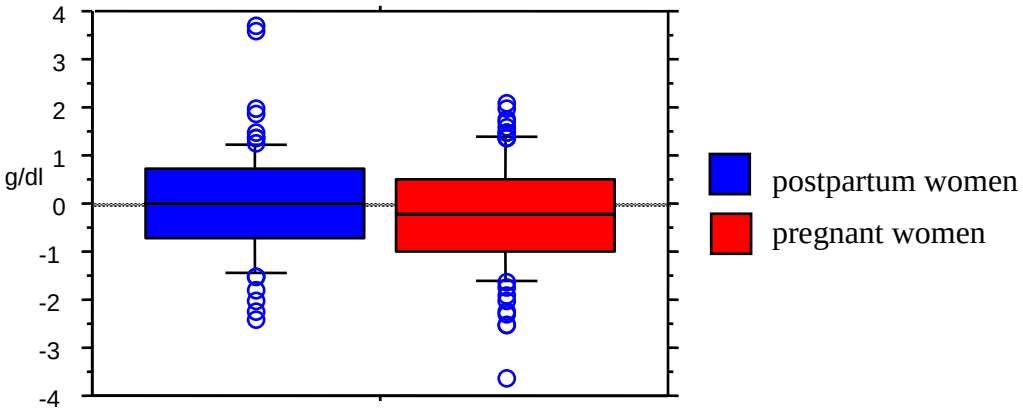
Table 2: Descriptive statistics of the differences of the haemoglobin estimates obtained by (medical student, nurse and patient) and haemoglobin estimate given by the goldstandard

	pregnant women	postpartum women	all
standard deviation (medical student)	1.09	1.09	1.09
standard deviation (nurse)	1.25	1.21	1.23
standard deviation (patient)	1.52	1.65	1.58
range (medical student)	-3.60/+2.10	-2.40/+3.70	-3.60/+3.70
range (nurse)	-3.60/+2.40	-3.30/+3.60	-3.60/+3.60
range (patient)	-4.70/+2.10	-4.80/+3.60	-4.80/+3.60
measured hb level, g/dl	12.04	11.24	11.72
estimated hb level, g/dl (medical student)	11.83	11.23	11.61
estimated hb level, g/dl (nurse)	11.77	10.83	11.40
estimated hb level, g/dl (patient)	11.34	10.31	10.93

The mean estimated haemoglobin level is fairly close to the mean measured haemoglobin level and there is a slight underestimation by all three examiners.

Relating to the standard deviation there is dissimilarity between the dispersion of the differences of the haemoglobin estimates between the examiners to the goldstandard haemoglobin estimates. The medical student has got a standard deviation of 1.09, the nurses of 1.23 and the patients of 1.58.

Figure 1: Box plot showing differences between medical student haemoglobin estimates versus goldstandard of postpartum women and pregnant women

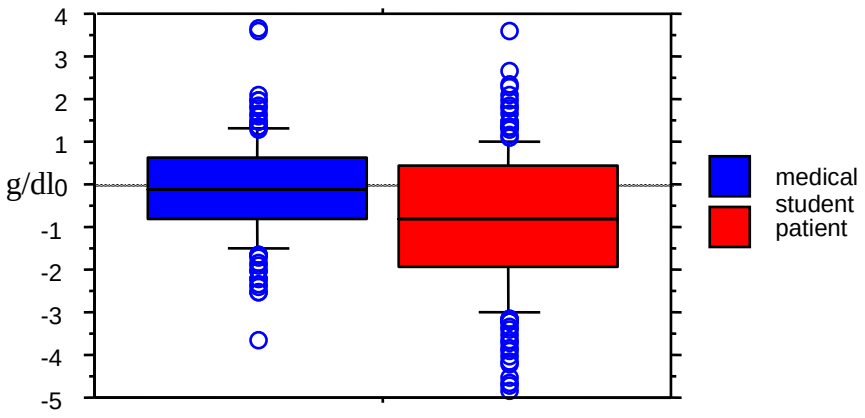


	Mean	Std. dev.	Minimum	Maximum	Median	IQR
all	-0.11	1.09	-3.6	3.7	-0.1	1.4
postpartum	0.04	1.09	-2.4	3.7	0.0	1.4
pregnant	-0.21	1.09	-3.6	2.1	-0.2	1.5

Mean estimated difference of the haemoglobin estimates of postpartum women and the haemoglobin estimates of the goldstandard is 0.04 and for pregnant women -0.21.

Standard deviation of the differences obtained by the medical student for postpartum women is 1.09 and for pregnant women 1.09.

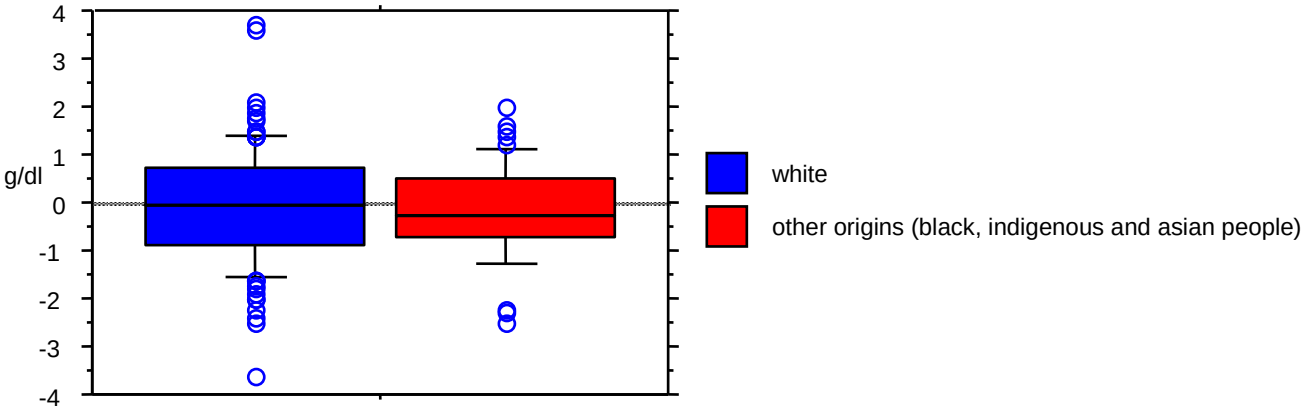
Figure 2: Box plot showing differences between medical student haemoglobin estimates versus goldstandard (all) and patient haemoglobin estimates versus goldstandard (all)



Comparison of variances between both groups shows significant differences of dispersion (P-value < 0.0001) whereas the patients reached a higher dispersion (1.58) than the medical student (1.09).

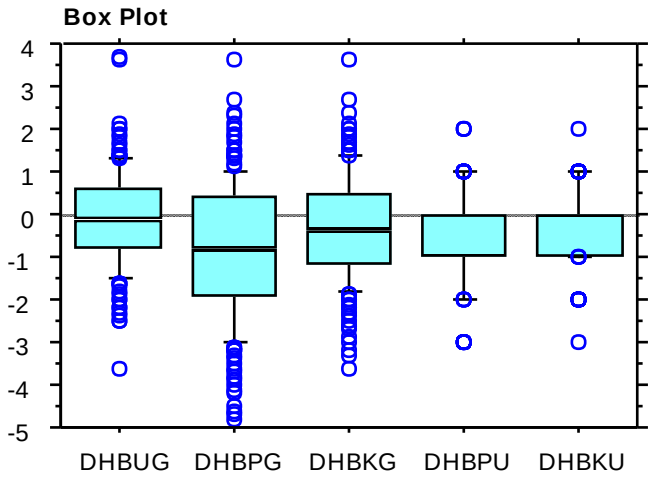
	Mean	Std. Dev.	Std. Error	Minimum	Maximum	Median	IQR
all	-0.45	1.40	0.06	-4.8	3.7	-0.35	1.8
medical student	-0.11	1.09	0.07	-3.6	3.7	-0.1	1.4
patient	-0.79	1.58	0.1	-4.8	3.6	-0.8	2.4

Figure 3: Box plot showing the differences between medical student haemoglobin estimates and the goldstandard haemoglobin estimates of postpartum women and pregnant women with white and other origins



Comparison of variances between both groups shows no significant differences of dispersion (P-value is 0.59). There is no larger dispersion for white origin.

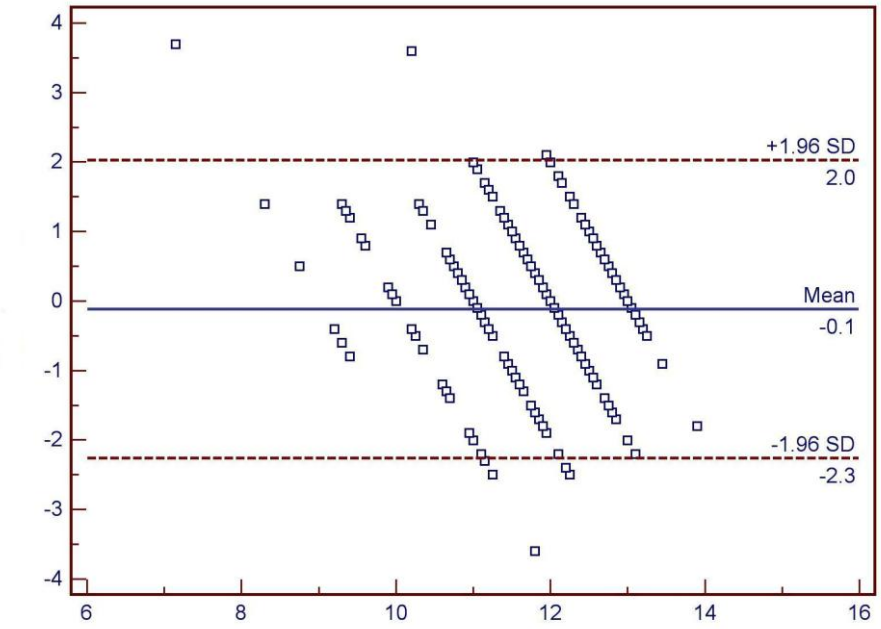
Figure 4: Box plot showing differences between haemoglobin estimates by medical student (DHBUG), patient (DHBPG) and nurse (DHBKG) versus goldstandard, patient versus medical student (DHBPU) and nurse versus medical student (DHBKU)



One sample t-test shows no differences between the estimation of the medical student versus goldstandard ($p = 0.1041$) but significant differences between all other groups ($p < 0.0001$). Medical student haemoglobin measurements have no bias with respect to the goldstandard haemoglobin estimates contrary to the other examiners.

	Mean	Std. Dev.	Minimum	Maximum
medical student	-0.11	1.09	-3.6	3.7
patient	-0.79	1.58	-4.8	3.6
nurse	-0.32	1.23	-3.6	3.6
patient/medical student	-0.68	1.11	-3.0	2.0
nurse/medical student	-0.21	0.86	-3.0	2.0

Figure 5: Bland-Altman plot showing all patients (pregnant and postpartum women)

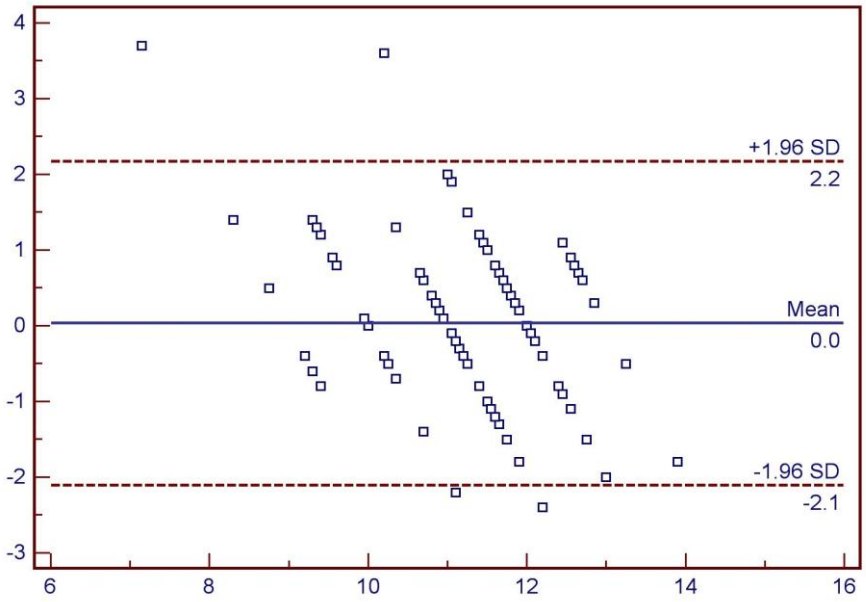


X-axis: mean of haemoglobin medical student and haemoglobin goldstandard

Y-axis: difference between haemoglobin medical student and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.3 and +2.0). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals -0.1.

Figure 6: Bland-Altman plot showing postpartum women

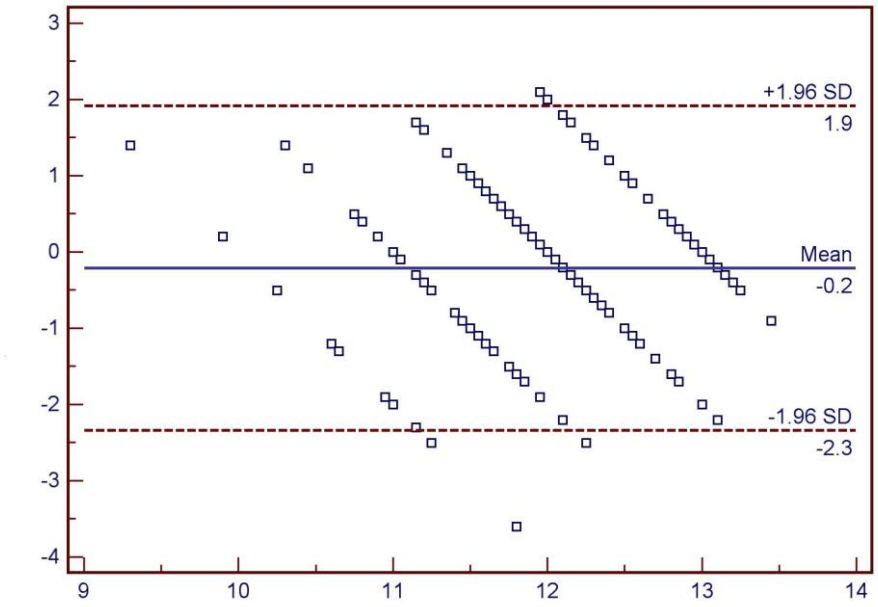


X-axis: mean of haemoglobin medical student and haemoglobin goldstandard

Y-axis: difference between haemoglobin medical student and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.1 and +2.2). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals 0.0.

Figure 7: Bland-Altman plot showing pregnant women

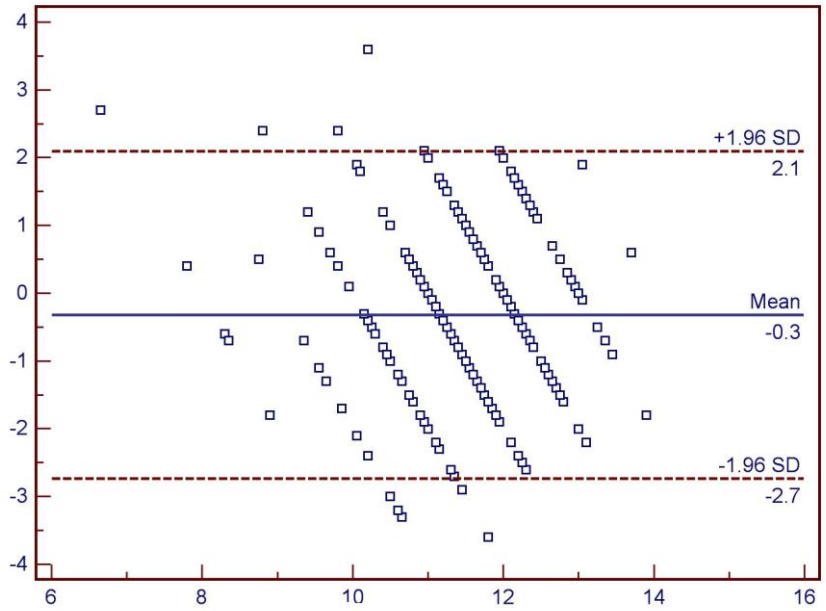


X-axis: mean of haemoglobin medical student and haemoglobin goldstandard

Y-axis: difference between haemoglobin medical student and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.3 and +1.9). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals -0.2.

Figure 8: Bland-Altman plot showing all patients (pregnant and postpartum women)

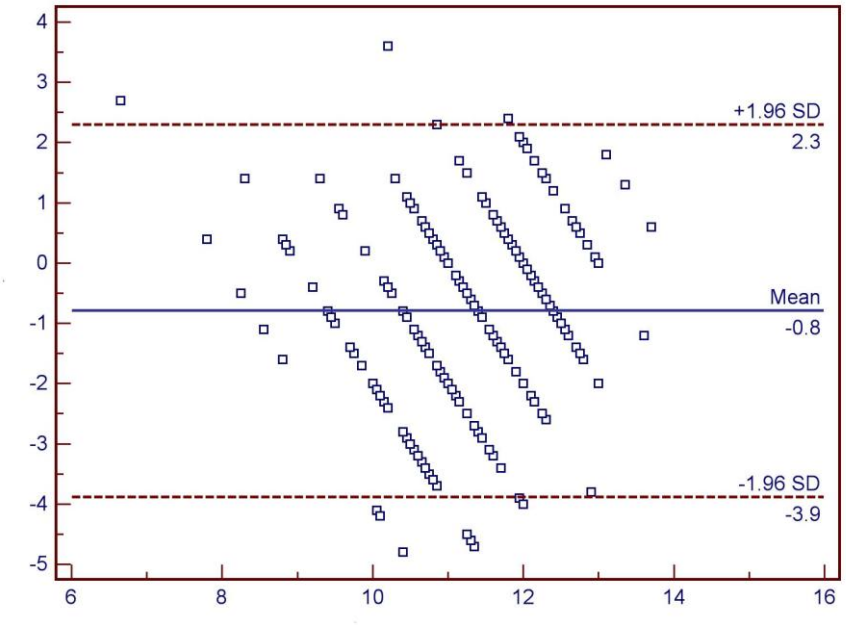


X-axis: mean of haemoglobin nurse and haemoglobin goldstandard

Y-axis: difference between haemoglobin nurse and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.7 and +2.1). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals -0.3.

Figure 9: Bland-Altman plot showing all patients (pregnant and postpartum women)



X-axis: mean of haemoglobin patient and haemoglobin goldstandard

Y-axis: difference between haemoglobin patient and haemoglobin goldstandard

95% of values are between the both dashed lines (-3.9 and +2.3). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals -0.8.

5. Discussion and Conclusion

5.1 Discussion

The tests of this simple non-invasive haemoglobin estimation for each patient were performed all together by three different examiners: first by the medical student, who was running the research, second by a random nurse and last by the patient herself.
The standard deviations of the differences of the haemoglobin measurements with respect to the haemoglobin measurements of the goldstandard of the three examiners are varying in a range of 1.09 to 1.58 g/dl (Figure 4 to 6). 95 % of the values of the medical student are in the range of - 2.3 and +2.0 to the goldstandard (Figure 1). Meanwhile it was - 2.7 and +2.1 for the nurses (Figure 4) and - 3.9 and +2.3 for the patients (Figure 7).
The standard deviations of the differences of the medical student and the patients were compared with each other and the P-Value was <0.0001, which is statistically significant (Figure 2).

In this study, the HemoHue® card was tested the first time on women in pregnancy and postpartum. Although a non-invasive test based on clinical signs without taking a blood sample is commonly used for anaemia detection (2, 4, 5), so far there exists no similar device to the tested card for measuring the degree of anaemia.
With a standard deviation of 1.09 to 1.58 of the differences of the haemoglobin values to the goldstandard haemoglobin estimates of the medical student and patients respectively, the measuring of blood with the HemoHue® card shows a clear tendency of the g/dl haemoglobin of a patient and the validity of this device is high enough to identify anaemic patients. The corresponding 95% limits of agreement are (-2.3 and +2.0) for medical student and (-3.9 and +2.3) for patients. It seems that they are good enough for the purpose of HemoHue® card. Medical student is the best, as the results were unbiased with respect to the goldstandard, however patients and nurses were biased.
Because the HemoHue® card is a non-invasive screening test, there is no need for taking a blood sample. Therefore, this method seems especially useful in village level settings where drawing blood is not possible and/or where cultural beliefs against blood drawing exist (4) (2). Another advantage is the fact that sophisticated methods for detection anaemia are too expensive for wide-spread use given the primary health care setting in most developing countries (6). The low production costs of the HemoHue® card as well as the minimum of

equipment needed to use it make this device a very cheap analyzing instrument. Therefore, the HemoHue® card may be widely distributed worldwide.

Furthermore, the origin of patients does not seem to influence the accuracy of the card. The tested women have been separated in white and other origins (black, indigenous and asian). There is no differences in the dispersion of the differences between white and other origin ($p = 0.59$) (Figure 3).

The results of the research are illustrated in Bland-Altman and Box plots. The dispersion of the discrepancy between different measurements is easy shown in these figures. Due to a small number of anaemic women (32), it is not trustworthy to interpret the sensitivity, specificity, positive predictive value and negative predictive value.

The research shows that the accuracy of the results and the usefulness of the HemoHue® card are depending on the user. There was a clear difference between the results of the medical student and of the patients.

The medical student obtained the best results among the examiners with a standard deviation of 1.09 g/dl haemoglobin (Figure 4). This can be explained by a learning effect during the research as the medical student was using the HemoHue® card over 252 times comparing to the patients who were using the HemoHue® card only once. Because the nurses were chosen randomly and – although some of them were using the card several times – they very likely did not experience the same learning effect as the medical student. Furthermore, the fact that the results depend on the personal skills of the examiner should be considered as well. It can be assumed that the personal ability of handling the HemoHue® card was different for each of the approximately 20 nurses who took part in the experiment. These two factors may explain the larger standard deviation of their results when compared with the medical student's. Nevertheless, it can be said that the results of the nurses are nearly as good as the ones of the medical student.

The patients themselves produced the least accurate results of the examiners. The fact that they had – in contrast to the medical student and the nurses – to look into a mirror in order to measure the most intensely colored spot of the conjunctiva can be considered as the main reason for their weaker performance. Further, their lack of any medical education could serve as another explanation. The medical student and the nurses could have in contrast a tendency to provide estimations near to a normal haemoglobin concentration.

Beware of the fact that the results depends on the examiner's interpretation of the colour of the conjunctiva, the method of the HemoHue® card is a subjective test (7). As confirmed in

other studies in which the haemoglobin was assessed, the subjectivity in perception of colour shades and pallor must be considered (13).
Another fact to be considered is that the HemoHue® card requires an adequate source of ambient light. This critical aspect can be solved with an integrated light calibration device that visualizes when the ambient light conditions are sufficient for proper use of the card. The first series of the HemoHue® studies showed the necessary of such an integrated light device. In one research, the light was not standardized in the beginning but only during the second term, the first results leaded to a bigger deviation to the goldstandard than the second.
Finally, any user of the HemoHue® card should always consider that with a standard deviation varying in a range of 1.09 to 1.58 g/dl haemoglobin to the goldstandard (Figure 4 to 6), the HemoHue® card is obviously not as accurate as a blood test.

Former studies of non-invasive assessment of anaemia in pregnancy showed the difficulties regarding the accuracy of the results. Especially the value of clinical symptoms (headache, dizziness, fatigue etc.) is at best doubtful because these symptoms are too common among all pregnant women in order to reliably define anaemic patients (2). In the longstanding practice of non-invasive clinical signs, the examination of the degree of pallor of the inner eyelid was part of the standard method to detect anaemia together with the colour of the lips, tongue, gums and the area under the fingernails. Usually, the colour of the conjunctiva was graded as “pink”, “pale” or “very pale” (6), “pale”, “slightly pale” or “not pale” (13) or classified in the categories “white”, “pink” and “red” (4). It was stated that the distinguishing of the colour shades was essential for the improvement of the accuracy of the non-invasive methods (4). This aspect was considered also in the invasive method called “filter paper method”. With a drop of blood on a filter paper the degree of anaemia can be assessed visually. The colour of the blood is compared against a colour chart (“WHO Haemoglobin Colour Scale”) (4, 6, 7).
The maintenance of equipment to detect anaemia is crucial to obtain accurate and consistent results (4). In developing countries, the costs for acquisition and maintenance of the apparatus to measure haemoglobin in a blood sample are often too high. Facilities to diagnose anaemia are limited (8). Most of the existing methods are expensive, complex or impractical for use in primary care in poor countries (9). As a consequence, in those poorest parts of the world where a high prevalence of anaemia exist, many patients cannot be detected (10). A simple, cost-effective way to detect the patients, who truly are in need of treatment, is essential (2).

5.2 Conclusion

The HemoHue® card is a simple, non-invasive device which can be used everywhere, including in non-clinical circumstances. The study showed a standard deviation of 1.09 g/dl haemoglobin by the results of the medical student as well as the standard deviation of 1.23 g/dl haemoglobin by the nurses. These results show that measurements by HemoHue® are good enough to get a fair estimate of the haemoglobin concentration of a patient. With this method, anaemia and a low haemoglobin level can be analyzed in pregnancy and during the postpartum period. As the examination led by patient does not show the same accuracy as the results of the medical student or the nurses, an informed and trained person is needed to run the analysis.

For developing countries, where laboratory facilities are limited and anaemia is highly prevalent (11), the HemoHue® card could therefore be a practical device for a quick and cost-effective analysis.

Because the study was run in Zurich, there were only few anaemic women in the sample. It would be useful to validate the findings in areas with higher prevalence of anaemia. Other factors such as the temperature or the weather could have an influence and may have to be considered, too.

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7. Appendix

7.1 Patient's informed consent

Schriftliche Einverständniserklärung der Probandin zur Teilnahme an einer klinischen Studie

- ***Bitte lesen Sie dieses Formular sorgfältig durch.***
- ***Bitte fragen Sie, wenn Sie etwas nicht verstehen oder wissen möchten.***

Nummer der Studie:	
Titel der Studie: Evaluation der „Anaemia Colour Scale" im Bereich der Geburtshilfe	
Ort der Studie: Universitätsspital Zürich	
Prüfarzt Name und Vorname: cand. med. dent. Dünner, Dominique und PD Dr. Breymann, Christian	
Probandin Name und Vorname:	
Geburtsdatum: (fakultativ)	Geschlecht: (fakultativ)
Gesetzlicher Vertreter der Probandin (falls Probandin unmündig und urteilsunfähig ist): Name und Vorname:	
Evtl. Verwandtschaftsgrad des Vertreters:	
Zeuge (nur in besonderen Fällen: Wenn Probandin z.B. schreibunfähig ist) Name und Vorname:	

- Ich wurde vom unterzeichnenden Arzt mündlich und schriftlich über die Ziele, den Ablauf der Studie mit dem *[Wirkstoff]*, über die zu erwartenden Wirkungen, über mögliche Vor- und Nachteile sowie über eventuelle Risiken informiert.
- Ich habe die zur oben genannten Studie abgegebene schriftliche Probandinneninformation vom *[Datum]* gelesen und verstanden. Meine Fragen im Zusammenhang mit der Teilnahme an dieser Studie sind mir zufriedenstellend beantwortet worden. Ich kann die schriftliche Probandinneninformation behalten und erhalte eine Kopie meiner schriftlichen Einverständniserklärung.
- Ich hatte genügend Zeit, um meine Entscheidung zu treffen.
- Ich bin darüber informiert, dass eine Versicherung Schäden deckt, falls solche im Rahmen der Studie auftreten.
- Ich bin einverstanden, dass die zuständigen Fachleute des Studienauftraggebers, der Behörden und der Ethikkommissionen zu Prüf- und Kontrollzwecken in meine Originaldaten Einsicht nehmen dürfen, jedoch unter strikter Einhaltung der Vertraulichkeit.
- Ich nehme an dieser Studie freiwillig teil. Ich kann jederzeit und ohne Angabe von Gründen meine Zustimmung zur Teilnahme widerrufen, ohne dass mir deswegen Nachteile bei der weiteren medizinischen Betreuung entstehen. In diesem Fall werde ich zu meiner Sicherheit abschliessend medizinisch untersucht.
- Ich bin mir bewusst, dass während der Studie die in der Probandinneninformation genannten Anforderungen und Einschränkungen einzuhalten sind. Im Interesse meiner Gesundheit kann mich der Prüfarzt jederzeit von der Studie ausschliessen. Zudem orientiere ich den Prüfarzt über die gleichzeitige Behandlung bei einem anderen Arzt sowie über die Einnahme von Medikamenten (vom Arzt verordnete oder selbständig gekaufte).

Ort, Datum	Unterschrift der Probandin
Ort, Datum	gegebenenfalls Unterschrift des gesetzlichen Vertreters
Ort, Datum	gegebenenfalls Unterschrift des Zeugen
Ort, Datum	Unterschrift des Prüfarztes

7.2 Patient information

Information für Versuchspersonen

Evaluation der „Anaemia Coulor Scale“ im Bereich der Geburtshilfe

Sehr geehrte Damen

Ihr behandelnder Arzt hat Ihnen vorgeschlagen an einer klinischen Studie teilzunehmen. Diese Studie verfolgt das Ziel, durch ein neues Hilfsmittel, eine Karte, die Hämoglobinkonzentration, die Zahl der Erythrozyten, im Blut zu bestimmen. Dies gibt Aufschluss über eine mögliche vorhandene Anämie. In diesem Schreiben finden Sie alle notwendigen Informationen betreffend diese Studie. Dies ermöglicht Ihnen die Entscheidung über die Teilnahme an diesen Vorhaben. Es ist Ihre ganz persönliche Wahl, diese Untersuchung zu vollziehen oder sie abzulehnen. Bei Gutheissung erhalten Sie eine schriftliche Einverständniserklärung zur Unterzeichnung.

Studienbeschreibung

Unter einer Anämie, das heisst Blutarmut, versteht man eine Verminderung der Hämoglobinkonzentration, Erythrozytenzahl (rote Blutkörperchen) und Hämatokrit. Die roten Blutkörperchen enthalten das Hämoglobin, ein Protein, das den Sauerstoff transportiert. Bei einer Anämie kommt es nun zu einer mangelhaften Sauerstoffversorgung des Körpers, da die Hämoglobinkonzentration vermindert ist.

Anämie in der Schwangerschaft und im Wochenbett kommt relativ häufig vor und birgt verschiedene Risiken für Mutter und Kind. Bei der Mutter stehen gehäufte Infektionen und das Risiko einer Frühgeburt im Vordergrund. Eine frühzeitige Diagnose ist deshalb sehr wichtig und wird durch regelmässige Blutentnahmen, die unter anderem den Hämoglobinwert messen, sichergestellt.

Die Messung der Hämoglobinmenge benötigt bei diesem Versuchsverfahren keine zusätzliche Blutentnahme. Die Anwendung der Karte ist einfach und birgt keine Risiken für Sie. Auf der Karte befinden sich einfach acht nummerierte Bilder, die einem Farbton des inneren Augenlides entsprechen. Das innere Augenlied verändert seine Farbe je nach Menge an Hämoglobin. Somit kann man den Farbton des inneren Augenliedes mit einer Farbe auf der Karte vergleichen und erhält dann seinen Hämoglobinwert. Je nach dem kann damit auf eine mögliche Anämie geschlossen werden.

Studienablauf

Nach Unterzeichnung der schriftlichen Einverständniserklärung erklärt der Untersucher den Ablauf dieser Studie. Anlässlich der regulären Blutentnahme wird der Hämoglobinwert routinemässig gleich mitbestimmt. Zudem wird das Augenlid mit der Farbskala auf der Karte von dem Untersucher verglichen. Den dadurch erhaltenen Wert kann nun mit dem Laborwert der Blutentnahme verglichen werden. Anschliessend werden Sie versuchen, selber Ihren Hämoglobinwert mittels der Karte vor einem Spiegel zu bestimmen.

Vertraulichkeit

Alle bei dieser Studie erhobenen Daten werden vertraulich behandelt. Die statistischen Auswertungen erfolgen gänzlich anonym. Die Resultate dieser Studie werden den zuständigen Gesundheitsbehörden mitgeteilt. Die Daten und Resultate dieser Studie können in wissenschaftlichen Formaten publiziert und präsentiert werden. Zudem können sie für zukünftige wissenschaftliche Untersuchungen verwendet werden. Alle die an dieser Studie beteiligten Personen unterstehen einer strikter Geheimhaltungspflicht und sind verpflichtet, keine Angaben, mittels denen die Identifikation einer Versuchsperson dieser Studie erfolgen kann, an Dritte mitzuteilen oder zugänglich zu machen.

Entschädigung, Kosten und Versicherung

Die Teilnahme an dieser Studie erfolgt ohne finanzielle Entschädigung und es fallen weder bei Ihnen noch bei Ihrer Krankenkasse Kosten an. Für die Durchführung dieser Studie wurde keine Versicherung abgeschlossen, da kein Risiko für die Schädigung der Gesundheit Ihrer Person besteht. Die Teilnahme oder Nichtteilnahme an dieser Studie hat für Ihre ärztliche Betreuung keinerlei Folgen.

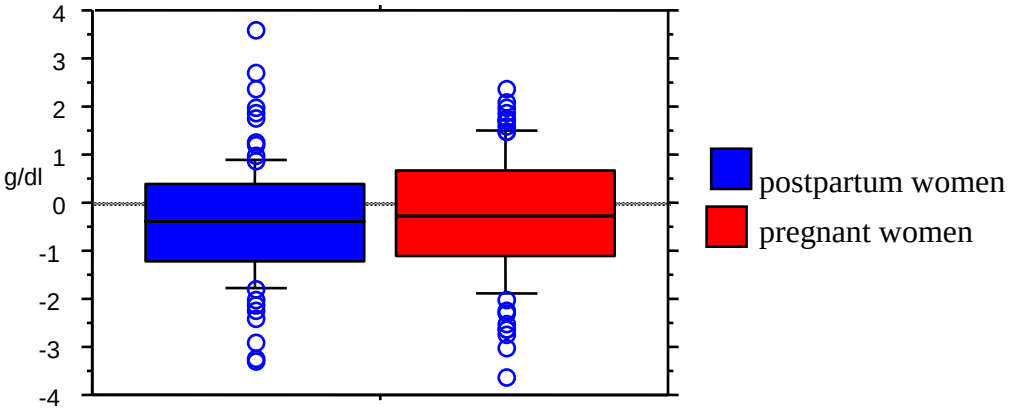
Kontaktpersonen

Für Fragen betreffend diese Studie steht Ihnen gerne Frau cand. med. dent. Dominique Dünner und Herr PD Dr. Christian Breymann, Universitätsspital Zürich, Frauenklinikstrasse 10, 8091 Zürich. Tel: 044 255 11 11 zur Verfügung.

Diese Studie wurde von der kantonalen Ethikkommission mit Beschluss im Juni 2007 genehmigt.
Zürich, 27. April 2007

7.3 Figures

Box Plot showing differences between nurses haemoglobin estimates versus goldstandard haemoglobin estimates of postpartum and pregnant women

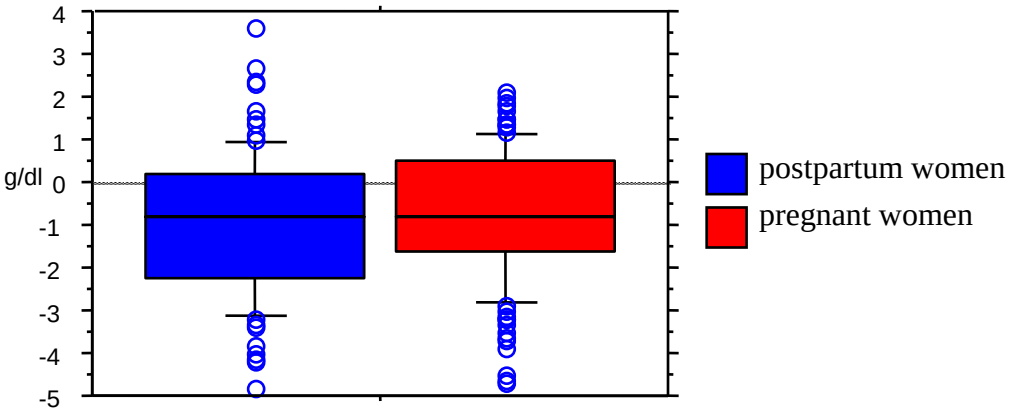


	Mean	Std. Dev.	Minimum	Maximum	Median	IQR
all	-0.32	1.23	-3.6	3.6	-0.4	1.7
postpartum	-0.41	1.21	-3.3	3.6	-0.4	1.6
pregnant	-0.26	1.25	-3.6	2.4	-0.3	1.8

Mean estimated difference of the haemoglobin estimates of postpartum women and the haemoglobin estimates of the goldstandard is -0.41 and for pregnant women -0.26.

Standard deviation of the differences obtained by the nurses for postpartum women is 1.21 and for pregnant women 1.25.

Box Plot showing differences between patients haemoglobin estimates versus goldstandard haemoglobin estimates of postpartum and pregnant women

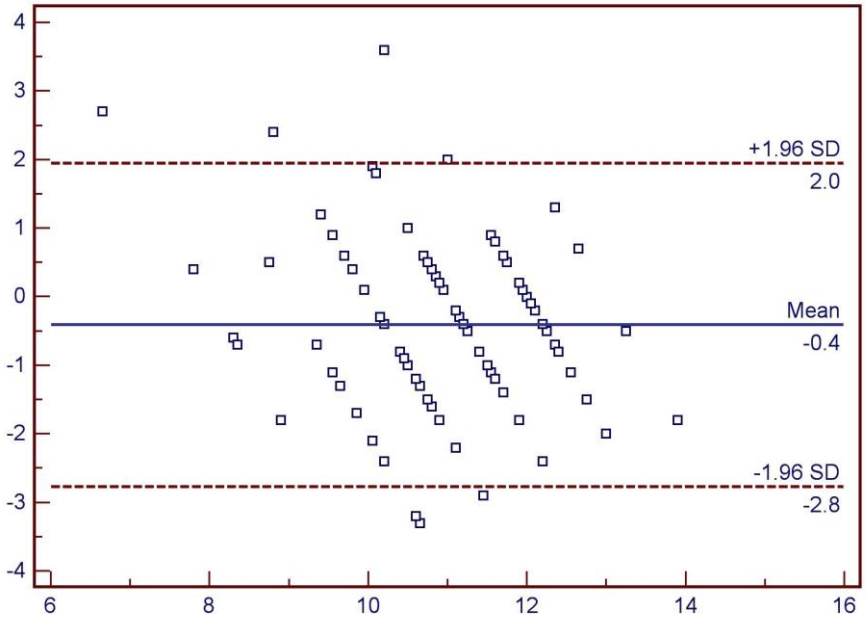


	Mean	Std. Dev.	Minimum	Maximum	Median	IQR
all	-0.79	1.58	-4.8	3.6	-0.8	2.4
postpartum	-0.94	1.65	-4.8	3.6	-0.8	2.4
pregnant	-0.69	1.52	-4.7	2.1	-0.8	2.1

Mean estimated difference of the haemoglobin estimates of postpartum women and the haemoglobin estimates of the goldstandard is -0.94 and for pregnant women -0.69.

Standard deviation of the differences obtained by patients for postpartum women is 1.65 and for pregnant women 1.52.

Bland-Altman plot showing postpartum women

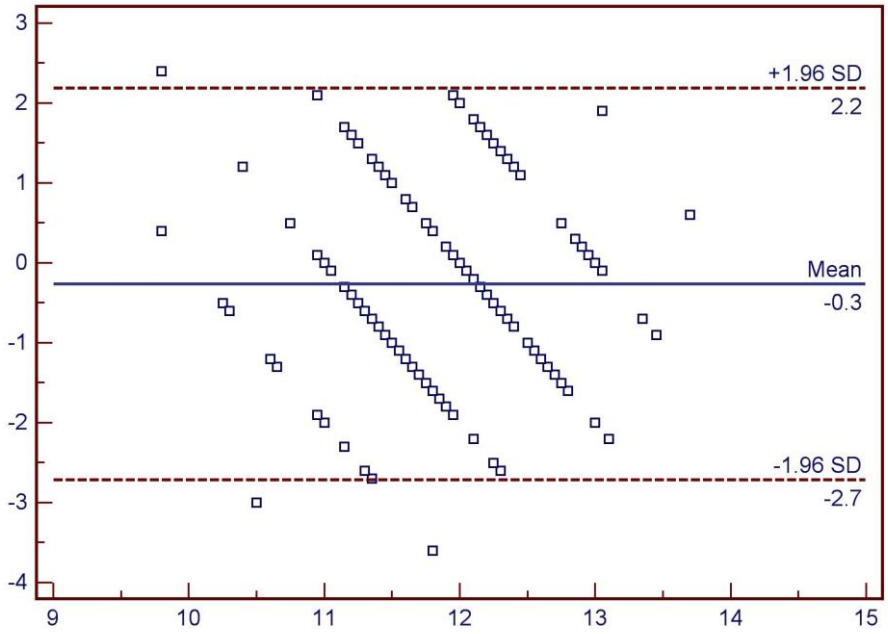


X-axis: mean of haemoglobin nurse and haemoglobin goldstandard

Y-axis: difference between haemoglobin nurse and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.8 and +2.0). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin nurse and haemoglobin goldstandard which equals -0.4.

Bland-Altman plot showing pregnant women

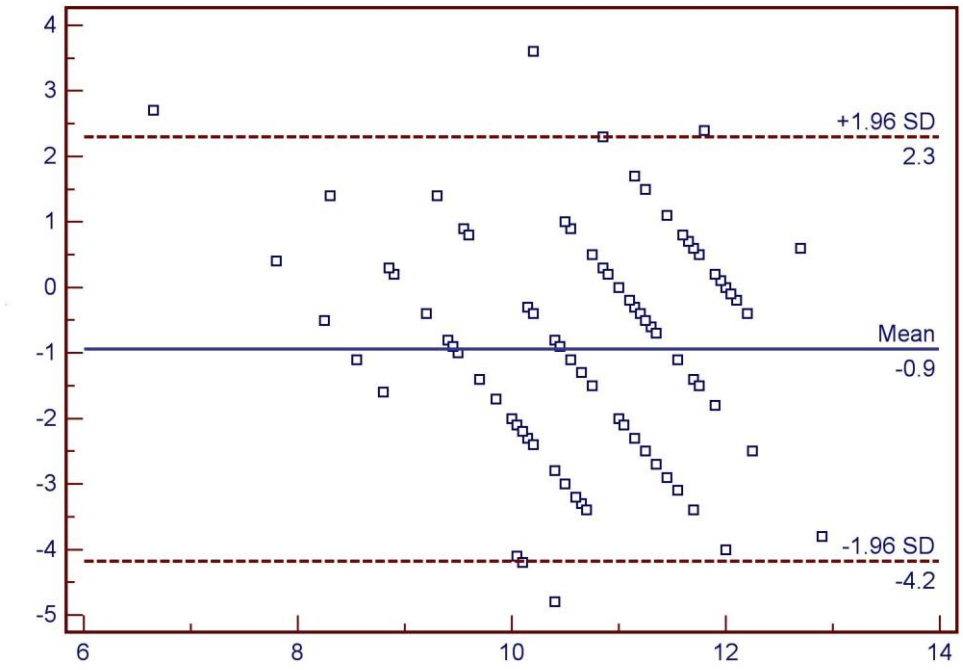


X-axis: mean of haemoglobin nurse and haemoglobin goldstandard

Y-axis: difference between haemoglobin nurse and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.7 and +2.2). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin nurse and haemoglobin goldstandard which equals -0.3.

Bland-Altman plot showing postpartum women

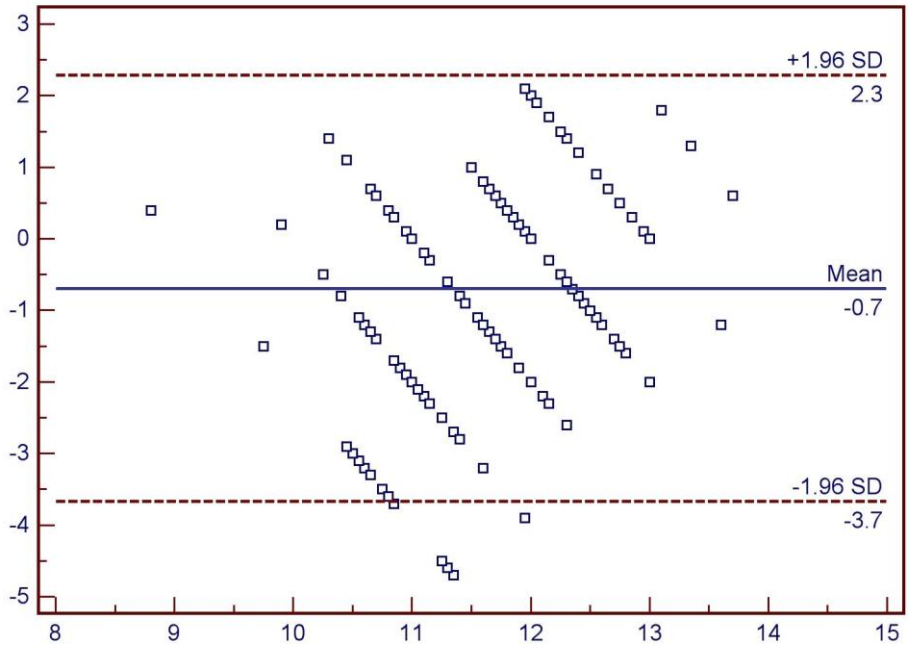


X-axis: mean of haemoglobin patient and haemoglobin goldstandard

Y-axis: difference between haemoglobin patient and haemoglobin goldstandard

95% of values are between the both dashed lines (-4.2 and +2.3). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin patient and haemoglobin goldstandard which equals -0.9.

Bland-Altman plot showing pregnant women

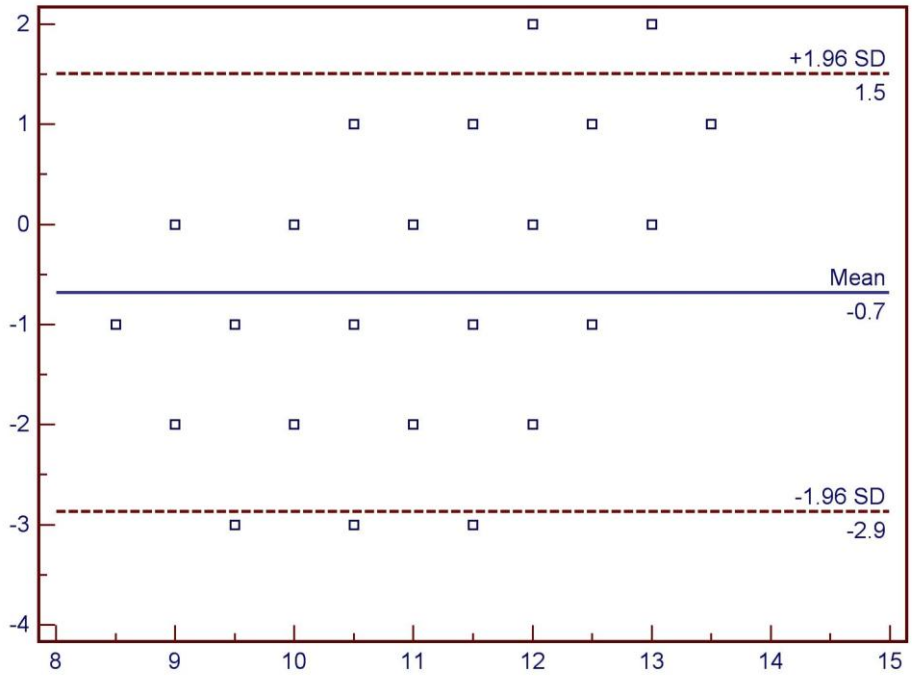


X-axis: mean of haemoglobin patient and haemoglobin goldstandard

Y-axis: difference between haemoglobin patient and haemoglobin goldstandard

95% of values are between the both dashed lines (-3.7 and +2.3). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin patient and haemoglobin goldstandard which equals -0.7.

Bland-Altman Plot showing all patients (pregnant and postpartum women)

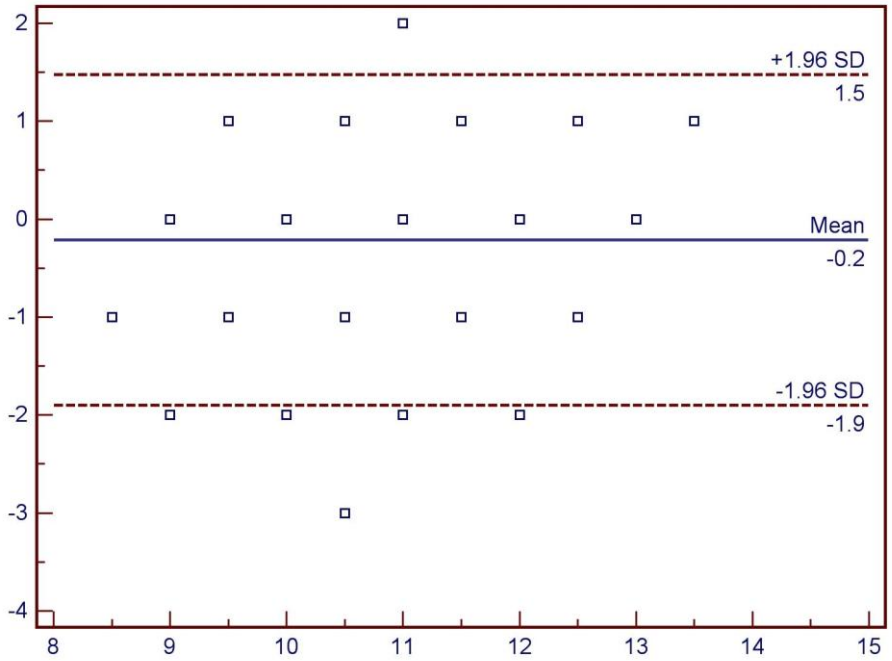


X-axis: mean of haemoglobin patient and haemoglobin medical student

Y-axis: difference between haemoglobin patient and haemoglobin medical student

95% of values are between the both dashed lines (-2.9 and +1.5). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin patient and haemoglobin medical student which equals -0.7.

Bland-Altman Plot showing all patients (pregnant and postpartum women)

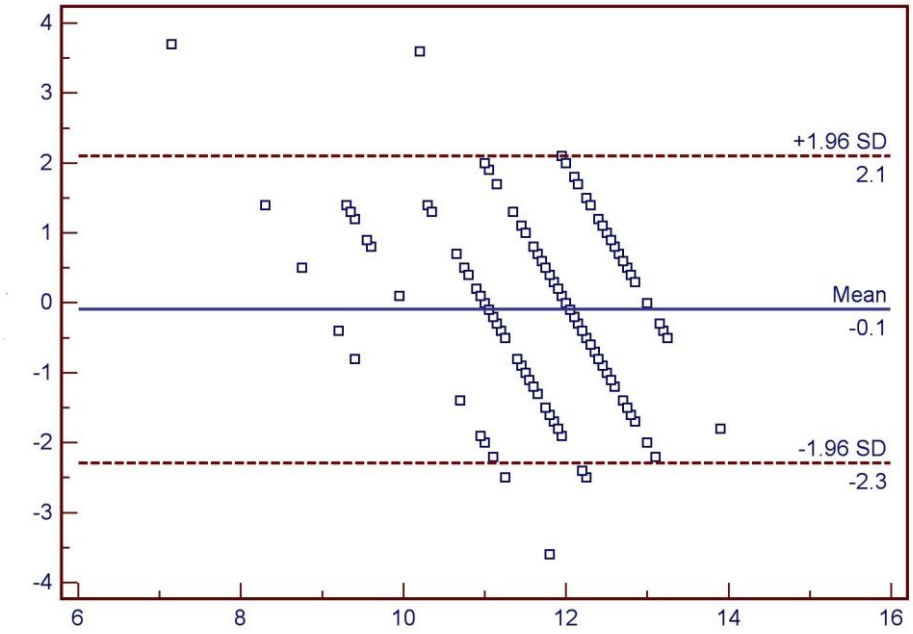


X-axis: mean of haemoglobin nurse and haemoglobin medical student

Y-axis: difference between haemoglobin nurse and haemoglobin medical student

95% of values are between the both dashed lines (-1.9 and +1.5). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin nurse and haemoglobin medical student which equals -0.2.

Bland-Altman Plot showing white patients (pregnant and postpartum women)

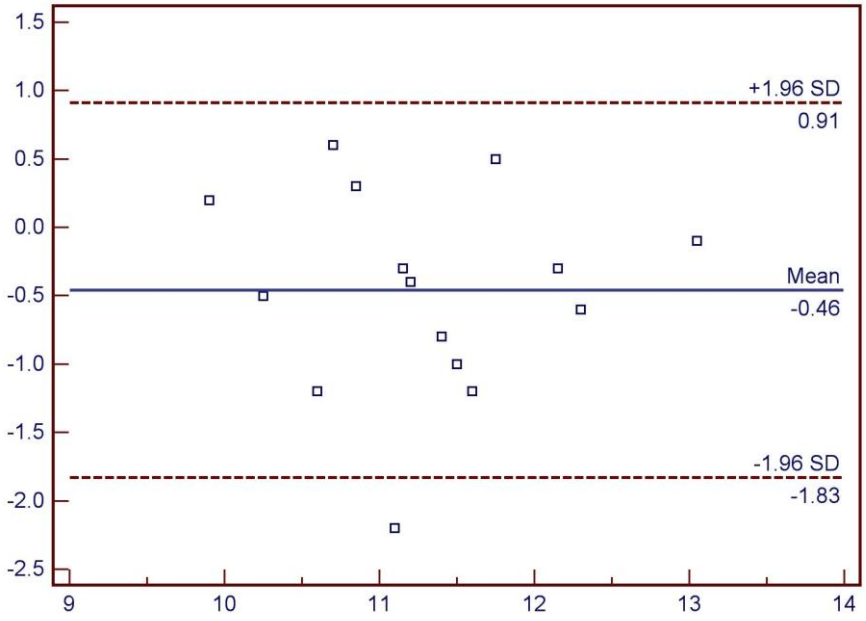


X-axis: mean of haemoglobin medical student and haemoglobin goldstandard

Y-axis: difference between haemoglobin medical student and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.3 and +2.1). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals -0.1.

Bland-Altman Plot showing black patients (pregnant and postpartum women)

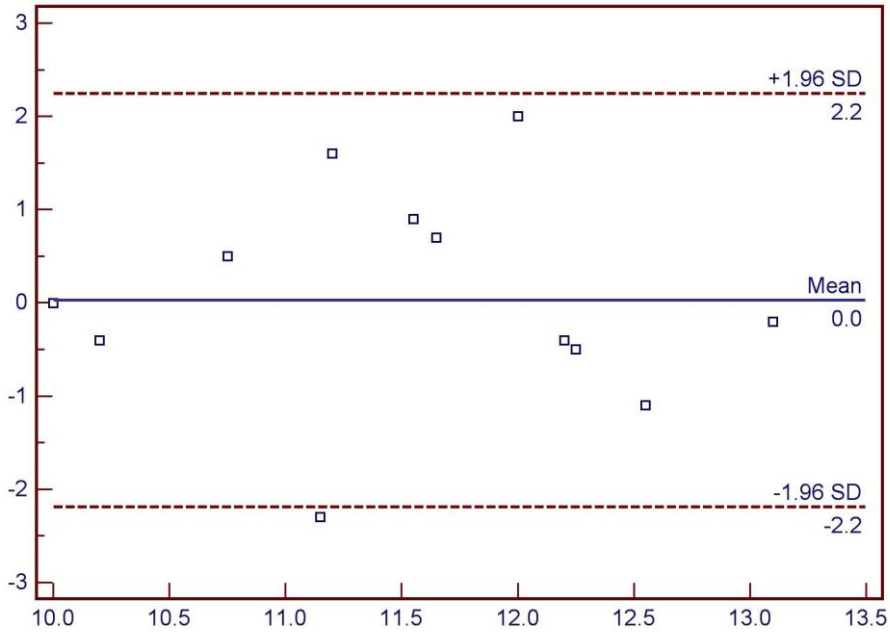


X-axis: mean of haemoglobin medical student and haemoglobin goldstandard

Y-axis: difference between haemoglobin medical student and haemoglobin goldstandard.

95% of values are between the both dashed lines (-1.8 and +0.9). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals -0.5.

Bland-Altman Plot showing indigen patients (pregnant and postpartum women)

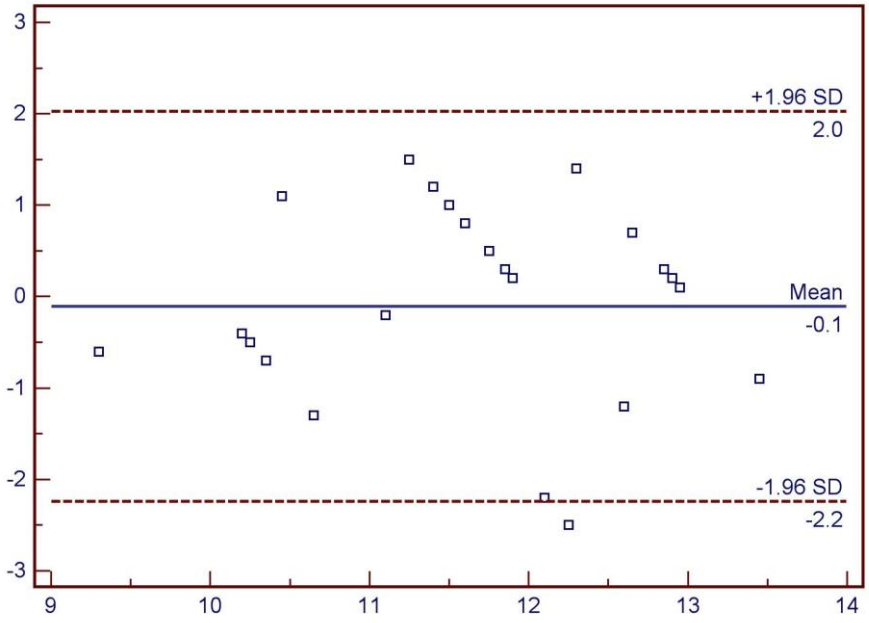


X-axis: mean of haemoglobin medical student and haemoglobin goldstandard

Y-axis: difference between haemoglobin medical student and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.2 and +2.2). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals 0.

Bland-Altman Plot showing asian patients (pregnant and postpartum women)



X-axis: mean of haemoglobin medical student and haemoglobin goldstandard

Y-axis: difference between haemoglobin medical student and haemoglobin goldstandard

95% of values are between the both dashed lines (-2.2 and +2.0). This range of values defines the 95% limits of agreement (3). The solid line represents the mean estimated value of the differences between haemoglobin medical student and haemoglobin goldstandard which equals -0.1.

Table: Sensitivity, specificity, positive predictive value and negative predictive value together with the 95% confidence interval (CI) for all women, for postpartum women and for pregnant women by the three examiners (medical student, nurses and patients)

Medical student	All (women), (%) (95% CI)	Postpartum women (%) (95% CI)	Pregnant women (%) (95% CI)
Sensitivity	34 (19;53)	44 (20;70)	25 (7;52)
Specificity	96 (93;98)	100 (96;100)	94 (89;97)
Positive predictive value	58 (34;80)	100 (59;100)	33 (10;65)
Negative predictive value	91 (87;94)	90 (83;96)	91 (85;95)

Nurses	All (women), (%) (95% CI)	Postpartum women (%) (95% CI)	Pregnant women (%) (95% CI)
Sensitivity	31 (16;50)	44 (20;70)	19 (6;43)
Specificity	92 (88;95)	92 (84;97)	93 (86;96)
Positive predictive value	37 (19;58)	50 (23;77)	23 (8;50)
Negative predictive value	90 (86;94)	90 (81;95)	91 (84;94)

Patients	All (women), (%) (95% CI)	Postpartum women (%) (95% CI)	Pregnant women (%) (95% CI)
Sensitivity	56 (38;74)	69 (41;89)	44 (20;70)
Specificity	75 (70;81)	78 (67;86)	75 (67;82)
Positive predictive value	25 (16;37)	37 (20;56)	17 (7;32)
Negative predictive value	92 (87;96)	93 (84;98)	92 (85;96)

Cut off value for pregnant women is 11 g/dl haemoglobin and 10 g/dl haemoglobin for postpartum women.